PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 16733	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International Application No. PCT/AU2003/001729	International Filing Date *(day/month/year)* 24 December 2003	Priority Date *(day/month/year)* 7 April 2003

International Patent Classification (IPC) or national classification and IPC

Int. Cl. [7] A61K 031/403; A61P 29/00

Applicant

JUROX PTY LTD et al

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 3 sheets, including this cover sheet.

   [X] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of **5** sheet(s).

3. This report contains indications relating to the following items:

I	[X]	Basis of the report
II	[ ]	Priority
III	[ ]	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	[ ]	Lack of unity of invention
V	[X]	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	[ ]	Certain documents cited
VII	[ ]	Certain defects in the international application
VIII	[ ]	Certain observations on the international application

Date of submission of the demand	Date of completion of the report
1 October 2004	4 May 2005
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **MICHAEL GRIEVE** Telephone No. (02) 6283 2267

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/AU2003/001729

Basis of the report

1. With regard to the **elements** of the international application:*

☐ the international application as originally filed.

☒ the description, pages **1 , 3 to 10** as originally filed,
pages , filed with the demand,
pages **2, 2A** received on **22 April 2005** with the letter of **22 April 2005**

☒ the claims, pages , as originally filed,
pages , as amended (together with any statement) under Article 19,
pages , filed with the demand,
pages **11 to 13,** received on **22 April 2005** with the letter of **22 April 2005**

☒ the drawings, pages **1/1,** as originally filed,
pages , filed with the demand,
pages , received on with the letter of

☐ the sequence listing part of the description:
pages , as originally filed
pages , filed with the demand
pages , received on with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages

☐ the claims, Nos.

☐ the drawings, sheets/fig.

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

I. **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Statement

Novelty (N)	Claims **1 to 22**	**YES**
	Claims	**NO**
Inventive step (IS)	Claims **1 to 22**	**YES**
	Claims	**NO**
Industrial applicability (IA)	Claims **1 to 22**	**YES**
	Claims	**NO**

2. Citations and explanations (Rule 70.7)

D1: AU 31470/99 B2 (762464) (& WO 1999/049845A1)

D2: WO 2001/060409A

D3: WO 2001/002015A

NOVELTY (N)

The invention as claimed in Claims 1 to 22 is considered to meet the criteria set out in PCT Article 33(2) as having novelty in light of the disclosure of documents D1 to D3. While these documents do disclose stable solvent-based compositions comprising carprofen, one or more polyols, one or more stabilising agents, and optionally one or more co-solvents in the same relative amounts as presently defined, and the use of such compositions in the treatment of pain and/or inflammation, these documents do not disclose solutions as presently defined. Rather, D1 discloses dispersion compositions (and specifically teaches away from solutions) and D3 relates to emulsion formulations, whereas the formulations of D2 require the use of certain components that are specifically excluded from the present invention.

As a result, Claims 1 to 22 are considered to be novel.

INVENTIVE STEP (IS)

Claims 1 to 22 – see the comments under novelty above.

Summary of the Invention

The present inventors have achieved stable solvent-based compositions of carprofen through the finding that certain solvent combinations with carprofen result in formulations that are stable and are suitable for oral administration to animals.

Accordingly, in a first aspect, the present invention is directed to a stable solution formulation consisting essentially of:
a therapeutically effective amount of carprofen;
one or more polyols;
one or more stabilising agents; and optionally,
one or more co-solvents.

In a second aspect, the present invention provides a stable solution composition consisting of:

a therapeutically effective amount of carprofen;

one or more polyols in an amount of from about 20 to 998g/L;

one or more stabilising agents in an amount of from about 0.1 to 50g/L; and

one or more co-solvents in an amount of from about 0 to 500g/L.

In a third aspect, the present invention is further directed to a method of treating pain and/or inflammation in a warm-blooded non-human animal, the method comprising administering to the animal a solution as defined in the first or second aspect.

In a fourth aspect, the present invention is further directed to the use of a mixture which consists essentially of:
one or more polyols;
one or more stabilising agents; and optionally,
one or more co-solvents,
to solubilise or stabilise carprofen and to facilitate the oral administration of a therapeutically effective amount of carprofen to a warm-blooded non-human animal.

In a fifth aspect, the present invention provides use of a composition consisting of:

one or more polyols;

one or more stabilising agents; and optionally,

one or more co-solvents,

to solubilise and stabilise carprofen and to facilitate the oral administration of a therapeutically effective amount of carprofen to a warm-blooded non-human animal.

In a sixth aspect, the present invention is still further directed to use of a therapeutically effective amount of carprofen which is solubilised in a mixture which consists essentially of:
one or more polyols;
one or more stabilising agents; and optionally,
one or more co-solvents.
in the preparation of a medicament for treating pain and/or inflammation in a warm-blooded non-human animal.

In a seventh aspect, the present invention provides use of a therapeutically effective amount of carprofen which is solubilised in a composition which consist of :
one or more polyols;
one or more stabilising agents; and optionally,
one or more co-solvents.
in the preparation of a medicament for treating pain and/or inflammation in a warm-blooded non-human animal.

Preferably, carprofen is included in the composition in an amount of about 1 to 500g/L, more preferably about 5 to 50 g/L, even more preferably about 20 to 50g/L. At these concentrations, an appropriately therapeutically effective amount of the composition may be administered to an animal.

CLAIMS:

1. A stable solution formulation consisting essentially of:
a therapeutically effective amount of carprofen;
one or more polyols in an amount of from about 20 to 998g/L;
one or more stabilising agents in an amount of from about 0.1 to 50g/L; and
one or more co-solvents in an amount of from about 0 to 500g/L.

2. A stable solution composition consisting of:
a therapeutically effective amount of carprofen;
one or more polyols in an amount of from about 20 to 998g/L;
one or more stabilising agents in an amount of from about 0.1 to 50g/L; and
one or more co-solvents in an amount of from about 0 to 500g/L.

3. The solution formulation according to claim 1 or claim 2 wherein the one or more polyols are selected from the group consisting of propylene glycol, glycerol, sorbitol, solid polyethylene glycols and liquid polyethylene glycols and mixtures of the foregoing; the one or more stabilising agents are selected from the group consisting of α tocopherol and salts thereof, ascorbic acid and salts thereof, methoxyphenol and derivatives thereof, trihydroxybenzoate and derivatives thereof, hydroquinone and derivatives thereof, methyl phenol and derivatives thereof, sodium metabisulfite and benzyl alcohol.

4. The solution formulation according to claim 1, 2 or 3 wherein the carprofen is in an amount of from about 1 to 500g/L.

5. The solution formulation according to claim 4 wherein the carprofen is in an amount of from about 5 to 50g/L.

6. The solution formulation according to any one of claims 1 to 5 wherein the one or more polyols are in an amount of from about 700 to 998g/L

7. The solution formulation according claim 6 wherein the one or more stabilising agents are in an amount of from about 10 to 20g/L.

8. The solution formulation according claim 6 or claim 7 wherein the one or more co-solvents are in an amount of from about 10 to 300g/L.

9. Use of a mixture consisting essentially of:
one or more polyols;
one or more stabilising agents; and optionally,
one or more co-solvents,
to solubilise and stabilise carprofen and to facilitate the oral administration of a therapeutically effective amount of carprofen to a warm-blooded non-human animal.

10. Use of a composition consisting of:
one or more polyols;
one or more stabilising agents; and optionally,
one or more co-solvents,
to solubilise and stabilise carprofen and to facilitate the oral administration of a therapeutically effective amount of carprofen to a warm-blooded non-human animal.

11. Use of a therapeutically effective amount of carprofen which is solubilised in a mixture which consists essentially of:
one or more polyols;
one or more stabilising agents; and optionally,
one or more co-solvents.
in the preparation of a medicament for treating pain and/or inflammation in a warm-blooded non-human animal.

12. Use of a therapeutically effective amount of carprofen which is solubilised in a composition which consist of :
one or more polyols;
one or more stabilising agents; and optionally,
one or more co-solvents.
in the preparation of a medicament for treating pain and/or inflammation in a warm-blooded non-human animal.

13. The use according to any one of claims 9 to 12 wherein the one or more polyols are selected from the group consisting of propylene glycol, glycerol, sorbitol, solid polyethylene glycols and liquid polyethylene glycols and mixtures of the foregoing; the one or more stabilising agents are selected from the group consisting of α tocopherol and salts thereof, ascorbic acid and salts thereof, methoxyphenol and derivatives thereof, trihydroxybenzoate and derivatives thereof, hydroquinone and derivatives thereof, methyl phenol and derivatives thereof, sodium metabisulfite and benzyl alcohol.

14. The use according to any one of claims 9 to 13 wherein the carprofen is in an amount of from about 1 to 500g/L.

15. The use according to claim 14 wherein the carprofen is in an amount of from about 20 to 50g/L.

16. The use according to any one of claims 9 to 15 wherein the one or more polyols are in an amount of from about 700 to 998g/L

17. The use according claim 16 wherein the one or more stabilising agents are in an amount of from about 10 to 20g/L.

18. The use according claim 16 or claim 17 wherein the one or more co-solvents are in an amount of from about 10 to 300g/L.

19. A method of treating pain and/or inflammation in a warm-blooded non-human animal, the method comprising administering to the animal a solution formulation as defined in any one of claims 1 to 8.

20. The method of claim 19 wherein the composition is administered orally.

21. A stable solution composition as any one embodiment hereinbefore described with reference to any one of Examples 1 to 7.

22. A method of treating pain and/or inflammation in a warm-blooded non-human animal as any one embodiment hereinbefore described with reference to any one of Examples 1 to 7.